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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

HM22/0317

NOVO NORDISK OF NORTH AMERICA INC
REZA GREEN
405 LEXINGTON AVENUE
SUITE 6400
NEW YORK NY 10174-6401

SLOBODYANSKY, E

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

03/17/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/325,603

Applicant(s)

Svensen et al.

Examiner
Elizabeth Slobodyansky

Group Art Unit
1652



☒ Responsive to communication(s) filed on Jan 19, 2000

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 71-75 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 71-75 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Interview Summary, PTO-413 (Paper #8)

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

The amendment filed January 19, 2000 amending the specification to correct typographical errors, amending claims 71 and 72 and adding claims 73-75 has been entered.

Claims 71-75 are pending.

The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Claims 71-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a variant of a parent α -amylase by modeling the parent α -amylase on an X-ray crystallographic three-dimensional structure of α -amylase having the amino acid sequence of SEQ ID NO:13 depicted in Appendix, does not reasonably provide enablement for a method of producing a variant of a parent α -amylase by modeling the parent α -amylase on an X-ray crystallographic three-dimensional structure of α -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, or having a sequence at least 70% homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13. The specification does not enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

This rejection in relation to claims 71 and 72 has been explained in the Office action mailed October 14, 1999. Newly added claims 73-75 include an additional step of modelling the parent α -amylase on a first modelled three-dimensional structure to produce a second modelled three-dimensional structure, wherein the first modelled structure is obtained by modeling an α -amylase on an X-ray crystallographic structure.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Factors pertinent to this discussion include predictability of the art, guidance in the specification, breadth of claims, and the amount of experimentation that would be necessary to use the invention.

In order to practice methods of claims 71-75 one skilled in the art would need an X-ray crystallographic three-dimensional structure of an α -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, and 13 or having a sequence at least 70%

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homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13. Although the specification teaches the X-ray crystallographic three-dimensional structure of α -amylase having amino acid sequence of SEQ ID NO: 13, it does not teach an X-ray crystallographic three-dimensional structure of an α -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, or having a sequence at least 70% homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13. The field of the enzyme X-ray crystallography requires highly specialized skills, and is highly unpredictable. The state of the art disclose an X-ray crystallographic three-dimensional structure of no bacterial α -amylase prior to the instant invention. In the prior art only the tree-dimensional structures of α -amylases from *Aspergillus oryzae*(SEQ ID NO:10 in the instant specification), barley and pig pancreas are known. In general, "[c]rystallization is usually quite difficult to achieve, and crystal growth can be slow; in some cases it may require months for sufficiently large crystals (0.5 mm) to grow from microcrystals. The formation of crystals is also critically dependent on a number of different parameters, including pH, temperature, protein concentration, the nature of the solvent and precipitant as well as the presence of added ions or ligands to the protein." (In Branden et al., page 271, 1st paragraph).

Therefore, one of ordinary skill would require the information regarding an X-ray crystallographic three-dimensional structure of an α -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, or having a sequence at least 70% homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13, in order to make steps required by

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methods of claims 71-75 and use methods of claims 71-75 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim 72 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 72 recites "an unrelated α -amylase". It is unclear which α -amylase can be considered unrelated.

In their Remarks filed January 19, 2000 Applicants refer to page 15, line 11-17 to define "an unrelated α -amylase" as "non-Termamyl-like- α -amylase". Since "Termamyl-like α -amylase" is defined as a *Bacillus* α -amylase (page 4, last paragraph through page 5, 1st paragraph), amending the claim to recite "a non-*Bacillus* α -amylase", for example, would be more clear.

Response to Arguments

In their Remarks filed January 19, 2000 regarding the enablement of a X-ray crystallographic structure", Applicants argue that "Applicants' success in crystallizing a representative α -amylase reflects the operability of the invention encompassing the use of a crystal structure of any α -amylase that is at least 70% homologous to SEQ ID Nos:

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2, 4, 6, or 13. This is supported by subsequent reported X-ray crystal structures, such as, e.g., by Machius et al., J. Mol. Biol. 246:545, 1995." (page 7, 1st full paragraph). These arguments have been fully considered but they are not persuasive. First, Applicants do not teach crystallization of any α -amylase. The specification provides the atomic coordinates only, i.e., the final result. Therefore, the process of crystallization of an α -amylase is not enabled. There is no direction in the specification guiding crystallization of any α -amylase. Furthermore, even conditions under which the crystal structure depicted in Appendix was obtained are not presented in the specification. As discussed, *supra*, crystallization is usually difficult to achieve, and the formation of crystals is also critically dependent on pH, temperature, etc. Second, subsequent disclosures such as Machius et al., even if they were using the teachings of the instant specification which they are not, do not make the prior work enabled.

The rejection of claims 71 and 72 under 35 U.S.C. 112, second paragraph, is withdrawn as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 72 under 35 U.S.C. 103(a) over MacGregor is withdrawn upon further consideration. Claim 72 requires the crystal structure of a *Bacillus* α -amylase. Said crystal structure can not be obvious because it is not enabled, as

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discussed *supra*. Therefore, the method of claim 72 drawn to the use of a crystal structure of a *Bacillus* α -amylase is non-obvious.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

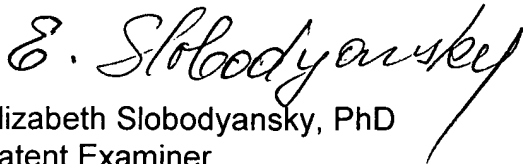
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script that reads "E. Slobodyansky". The signature is written in black ink and is positioned above the printed name and title.

Elizabeth Slobodyansky, PhD
Patent Examiner

March 14, 2000